REMARKS

Status of Claims

Prior to entry of this paper, claims 1, 3, 5, 10-11, 14-15, 17-19, 21-24, 27-30, and 33-45, 47-63, and 86-101 were pending. Claims 44-45, 47, 60, and 95-100 are canceled herein. Claims 1, 11, 33, and 101 are amended herein. New claims 102-109 are presented herein.

After entry of this paper, claims 1, 3, 5, 10-11, 14-15, 17-19, 21-24, 27-30, and 33-43, 48-59, 61-63, and 86-94, and 101-109 are pending. Of the pending claims, claims 19, 21-24, 27-30, 33-39, and 41 (corresponding to Groups II and III in the Restriction Requirement of July 25, 2008) are withdrawn by the Examiner. Applicants reserve the right to pursue any canceled subject matter in one or more related applications.

Support for Amendments

Claim 1 is amended wherein "said composition is stabilized with dry heat at 110-200°C." Support can be found throughout the specification as filed, for example at paragraphs [0026], [0033], [0108], [0150], and as a preferred method in paragraph [0162] (paragraph citations refer to the paragraph numbering the corresponding publication US 2007/0009578).

Claim 11 is amended to remove the term "USP 24." Support for the amendment can be found throughout the specification as filed, for example at paragraph [0063].

Claim 33 is amended to reflect a preferred embodiment. Support for the amendment can be found throughout the specification as filed, for example in original claim 33.

Claim 101 is amended to include the term "cross-linked" and wherein "said haemostatic composition does not comprise a chemical cross-linking agent or residues thereof." Support can be found throughout the specification as filed, for example at paragraphs [0040], [0044], [0093],

[0094], [0119], [0131], [0157], [0162], and [0169]. An embodiment of the invention not including a chemical cross-linking agent is described, for example, at [0094], where the specification states that in a preferred embodiment, "the haemostatic sponge of the present invention does not comprise a chemical cross-linking agent," [0094]. See also [0119].

New claims 102-109 are added. Support can be found throughout the specification as filed, for example, at paragraphs [0053], [0040], [0110], [0111], [0036], [0098], [0063], and in claims 1, 10, 16, and 101.

Support for the exclusion of a chemical cross-linking agent can be found in the specification as filed, for example at paragraphs [0094] and [0119].

No new matter is introduced.

Objections

The Office Action objects to the specification for failing to provide antecedent basis for claims 44 and 47. Applicants respectfully traverse. However, as claims 44 and 47 are canceled, Applicants respectfully request withdrawal of the objection as moot.

The Office Action objects to claim 11 for the term "USP 24." Applicants respectfully traverse. However, as the claim is amended to remove the term, Applicants respectfully request withdrawal of the objection as moot.

Rejection Under 35 USC § 112, 2nd paragraph

The Office Action rejects claims 1 and 11 (and dependent claims 3, 5, 10, 14-15, 17-18, 42-45, 47-63, and 86-101) under 35 USC § 112, 2nd paragraph.

Claim 1 is rejected for the term "thereof" as being indefinite for being unclear as to whether the term refers to gelatin or hyaluronic acid. Applicants respectfully traverse the rejection, and submit that the claim is sufficiently clear to a hypothetical person possessing the ordinary level of skill in the pertinent art, which is the standard required by 35 USC § 112, 2nd paragraph. Applicants further note that, according to the MPEP, "[s]ome latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire" (MPEP 2173.02). Nevertheless, in order to advance prosecution, Applicants amend the punctuation and spacing in claim 1. Applicants believe the change in punctuation and spacing renders the rejection moot.

Claim 11 is rejected for the term USP 24. Applicants respectfully traverse the rejection. However, Applicants believe the amendment to claim 11 renders the rejection moot.

Rejection Under 35 USC § 102(b)

The Office Action rejects claims 1, 3, 5, 10, 11, 17, 40, 42-45, 47, 51, 57, 60-63, 86, 89, 92, 95, 98, and 101 under 35 USC § 102(b) as being anticipated by Choi et al (J. Biomed. Mater. Res.). Applicants respectfully traverse the rejection for at least the reason that Choi does not disclose the currently claimed features.

The Federal Circuit has held that "[A]nticipation under § 102 can be found only when the reference discloses exactly what is claimed and that where there are differences between the reference disclosure and the claim, the rejection must be based on § 103 which takes differences into account." *Titanium Metals Corp. v. Banner*, 778 F.2d 775 (Fed. Cir. 1985).

With regard to claims 1, 40, 42, 43, new claim 103, and the claims dependent therefrom, the claims recite haemostatic compositions comprising gelatin and hyaluronic acid or a

derivative of hyaluronic acid, where the haemostatic composition is stabilized with dry heat at 110-200°C. Choi fails to anticipate claims 1, 40, 42, 43, and new claim 103 (and the claims dependent therefrom) because Choi fails to disclose gelatin and hyaluronic acid treated with dry heat, let alone treatment with dry heat at a temperature 110-200°C. While the Office Action asserts on page 4 that Choi teaches physical cross-linking by thermal heating, this is not actually the case. Choi actually mentions physical cross-linking by thermal heating in the context of gelatin only (see Choi, p. 631, last paragraph). In fact, Choi discloses compositions that are cross-linked by a chemical agent such as EDC (see Choi, Materials and Methods, p. 632). As such, claims 1, 40, 42, 43, and new claim 103 (and the claims dependent therefrom) are novel over Choi.

With regard to claim 101, the claim is directed to a cross-linked haemostatic composition comprising gelatin and hyaluronic acid (HA), or a derivative thereof, wherein said hyaluronic acid (HA), or a derivative thereof, is incorporated into said composition to a final content of at least 10% (w/w) and at most 90% (w/w), and wherein said gelatin is incorporated into said composition to a final content of at least 10% (w/w) and at most 90% (w/w), and wherein said composition does not comprise a chemical cross-linking agent or residues thereof. Similarly, new claims 102-109 all include the limitation wherein the composition of the claim does not comprise a chemical cross-linking agent or residues thereof. Choi specifically states that the gelatin and HA must be cross-linked (p. 631, col. 2), and discloses the use of a chemical cross-linking agent such as EDC (p. 632, col. 2). As such, Choi fails to anticipate claim 101 and new claims 102-109.

Rejection Under 35 USC § 103(a)

The Office Action rejects claims 1, 3, 5, 10, 11, 14, 15, 17-18, 40, 42-45, 47-63, and 86-101 under 35 USC § 103(a) as being obvious in view of the combination of Choi et al (J. Biomed. Mater. Res.), Della Valle et al (US Patent No. 4,851,521) and Moore et al (US Patent No. 3,678,933). Applicants respectfully traverse for at least the reason that the references, either individually or in combination, fail to teach all of the claimed features.

U.S. case law holds that a proper obviousness inquiry requires four factual inquiries: (a) determining the scope and contents of the prior art; (b) ascertaining the differences between the prior art and the claims in issue; (c) resolving the level of ordinary skill in the pertinent art; and (d) evaluating evidence of secondary consideration. See *Graham v. John Deere*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). Although the Supreme Court in *KSR* recently rejected a rigid application of the "teaching, suggestion, motivation" test, the Court did recognize that a showing of "teaching, suggestion, or motivation " to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a). See *KSR Int'l Co. v. Teleflex, Inc.*, No 04-1350 at 15 (U.S. Apr. 30, 2007). The Court further noted that an analysis supporting a rejection under 35 U.S.C. § 103(a) should be made explicit, and that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR*, slip op. at 14.

As discussed above, Choi fails to disclose gelatin and hyaluronic acid treated with dry heat, let alone treatment with dry heat at a temperature 110-200°C. Rather, Choi discloses compositions that are cross-linked by a chemical agent such as EDC (see Choi, Materials and Methods, p. 632). While the Office Action asserts on page 4 that Choi teaches physical cross-

linking by thermal heating, this is not actually the case. Choi actually mentions physical cross-linking by thermal heating in the context of gelatin only (see Choi, p. 631, last paragraph). Moreover, one of ordinary skill in the art would not find it obvious to use dry heat at temperatures of 110-200°C to cross-link gelatin and HA, because as described in the specification at paragraph [0109], HA is generally considered unstable at high temperatures. Therefore, the disclosure of Choi fails to provide a teaching of gelatin and hyaluronic acid treated with dry heat, let alone treatment with dry heat at a temperature 110-200°C, or alternatively, Choi fails to teach a composition that does not comprise a chemical cross-linking agent or residues thereof. As neither Della Valle nor Moore remedy this core deficiency in Choi, Applicants respectfully request that the rejection be withdrawn.

In addition to the fact that the cited references fail to teach all of the claimed features, Applicants have surprisingly found that the gelatin/HA or derivative thereof sponges of the present invention retain activity when treated with dry heat at 110-200°C, and the use of such sponges leads to a reduction in bleeding intensity compared to conventional gelatin sponges, as described in paragraph [0109] and Example 6 of the specification. The present inventors have found that treating a gelatin/HA or derivative thereof sponge with dry heat at 110-200°C confers several advantages, including sterilization of the haemostatic composition, stabilization of the three-dimensional sponge structure, and the absence of residues of chemical cross-linking agents.

Moreover, compositions according to the invention can be conveniently prepared in a one-step process, rendering additional steps for sterilization and/or removal of toxins unnecessary. Contrast this with the sponge disclosed in Choi, which requires sterilization with ethylene oxide (EO) gas for 6 hours, followed by aeration for at least 24 hours (page 632-633). In addition, EO is a carcinogenic substance, making its use in a medical compositions

problematic. The problem of toxicity of EO is compounded by the fact that chemical cross-linking agents as taught by Choi are also toxic (see Choi, p. 632, col. 1).

Clearly, the sponge of the present invention differs from the teachings of Choi, and such differences are not bridged by the teachings of Della Valle and Moore. Moreover, a sponge according to the present invention is surprisingly superior to the prior art in that the sponge according to the present invention surprisingly maintains effectiveness despite treatment with dry heat at 110-200°C, and as such, the sponge of the present invention avoids chemical cross-linking agents and their residues.

Product by Process

The Office Action asserts that the sponge obtained by Choi with chemically cross-linked gelatin/HA is identical to or only slight different from the product claimed in the product-by-process claims of the present invention (claims 40, 42, and 43, and any new or amended claims with the 110-200°C). Applicants respectfully traverse for at least the reason that the sponge of Choi would necessarily contain chemical cross-linking agents or their residues. These are undesirable for medical uses, and would be easily measured or quantified via laboratory testing. In contrast, the products of the instant process would be free of toxic residues as well as being free of endotoxins[1] released by bacteria during sterilization with ethylene oxide as taught by Choi. Therefore, for least the reason that the product by process claims would necessarily produce a product with important differences from the product taught by Choi, Applicants

[1] Endotoxins are understood to be structural components of bacteria that are mainly released when bacteria are lysed.

respectfully request withdrawal of the Examiner's comments with respect to product-by-process claims.

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided.

AUTHORIZATION

The Commissioner is hereby authorized to charge any fees which may be required for this amendment, or credit any overpayment to Deposit Account No. **50-3732**, Order No. **13323.105005**. Furthermore, in the event that an extension of time is required, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to the above-noted Deposit Account No. **50-3732** and Order No. **13323.105005**.

Respectfully submitted,
KING & SPALDING, L.L.P.

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By: /michael willis/
Jonathan D. Ball / Michael A. Willis
Reg. No. 59,928 / Reg. No. 53,913

KING & SPALDING, L.L.P.
1185 Avenue of the Americas
New York, New York 10036-4003
(212) 556-2115 (212) 556-2222 (Fax)